Creutzfeldt-Jakob Disease (CJD)
Table of Contents

Creutzfeldt-Jakob Disease (CJD)

Overview [1,2,5]

Creutzfeldt-Jakob disease is a rare, fatal brain disorder that causes a rapid, advancing dementia and associated muscle and nerve disturbances. The disease is often referred to as a subacute spongiform encephalopathy because it usually produces microscopic (sponge-like) holes in the brain (the disease is also referred to as transmissible spongiform encephalopathy or TSE). The human TSEs include: CJD, Gerstmann-Stäussler-Scheinker syndrome (GSS), kuru, Alper's syndrome, and Fatal familial insomnia. The infectious agents are thought to be unique proteins generally referred to as prions.

CJD is the most common of the human prion diseases. Typically, CJD onsets in later life and occurs at approximately 1 case per million annually, worldwide. CJD has four different categories: sporadic (spontaneous), iatrogenic (associated with medical use of infected pituitary-derived hormones and dura mater), familial (inherited), and variant CJD, which is thought to be associated with dietary consumption of tissue from cattle infected with bovine spongiform encephalopathy. For a more complete description of CJD, refer to the following texts:

- Control of Communicable Diseases Manual (CCDM)
- Red Book, Report of the Committee on Infectious Diseases.
- Mandell, Douglas and Bennett's *Principles and Practice of Infectious Diseases*

Case Definition [3]

1. Sporadic CJD (sCJD):

Confirmed:

- Diagnosed by standard neuropathological techniques (biopsy and/or autopsy), and/or
- Immunocytochemically, and/or
- Western blot confirmed protease-resistant PrP, and/or
- Presence of scrapie-associated fibrils.

Probable:

Progressive dementia and at least two of the following four clinical features:

- Myoclonus – seizure-like severe muscle contractions.
- Visual or cerebellar signs – double or blurred vision, and/or inability to visually recognize familiar objects.
- Pyramidal/extrapyramidal signs – poor control or poor initiation of skilled movement (primarily hands and fingers), poor control of speech, and difficulty forming words.
- Akinetic mutism - no spontaneous movement or attempt to formulate speech.

And

- Atypical EEG during an illness of any duration and/or a positive 14-3-3 CSF assay and a clinical duration to death of less than two years.
- Routine investigations do not suggest an alternative diagnosis.

Suspect:

- Death certificate indicating CJD as a cause of death (this means the mention of CJD anywhere on the death certificate), or
- Progressive dementia and at least two of the following four clinical features:
  -Myoclonus.
  -Visual or cerebellar signs.
  -Pyramidal/extrapyramidal signs.
  -Akinetic mutism.
  -And
  -No EEG performed or atypical EEG and duration to death of less than two years.

2. Iatrogenic CJD (iCJD) (or Acquired CJD [4]):

- Progressive cerebellar syndrome in a recipient of human cadaveric-derived pituitary hormone, or
- Sporadic CJD with a recognized exposure risk, (e.g., antecedent neurosurgery with dura mater implantation.)

3. Familial CJD (fCJD):

Confirmed or probable CJD plus confirmed or probable CJD in a first degree relative, and/or
neuropsychiatric disorder plus disease-specific PrP gene mutation.

4. Variant CJD (vCJD) or (nvCJD[4]):

Neuropathological diagnosis is mandatory for confirmation of suspected vCJD. Confirmatory examination of the brain should show the following neuropathological features:

- Numerous widespread amyloid plaques surrounded by vacuoles.
- Spongiform change most evident in the basal ganglia and thalamus.
- Prion protein accumulation in high density shown by immunocytochemistry, particularly in the cerebellum.

As with sCJD, the patient is suspect for vCJD when the patient's history reveals a rapid dementia and observed loss of muscle coordination. Tonsil biopsy may show prion protein scrapie isoform (PrPSc). Confirmation of the disease is done through brain biopsy or autopsy.

Information Needed for Investigation

Verify the diagnosis. Obtain a copy of the CD-1 or death certificate. What laboratory tests were conducted? If a biopsy and/or an autopsy was performed, obtain results. If laboratory tests were not conducted, are specimens available? What are/were the patient's clinical symptoms?

Establish the extent of illness. Early onset of CJD should prompt a thorough search for iatrogenic sources of infection and is characteristic of some cases of vCJD and fCJD[(5)]**.**

Contact the Regional Communicable Disease Coordinator immediately if vCJD is suspected.

Case Follow Up and Control Measures

- **Cases 54 years of age or younger diagnosed with CJD – deceased.** Perform a chart extraction and obtain copies of the following:
  1. Discharge summary
  2. Neurology consultation notes
  3. Psychiatric consultation notes
  4. EEG reports
  5. MRI reports
  6. Pathology report from brain biopsy or autopsy

- **Cases 54 years of age or younger diagnosed with CJD – not deceased.** Obtain as much of the above information as is available. If diagnostic laboratory testing has not been performed, inform the physician that laboratory services are available from:

  National Prion Disease Pathology Surveillance Center (NPDPSC)
  Institute of Pathology, Room 419
  Case Western Reserve University
  2085 Adelbert Road
  Cleveland, Ohio 44106
  Phone: 216-368-0587

  The laboratory can perform testing on biopsies of brain tissue, CSF, and blood. Refer to their web site for more information: **http://www.cjdsurveillance.com** (4/05)

- **Cases 55 years of age or older diagnosed with CJD – deceased.** Determine if an autopsy/biopsy or other diagnostic pathology was performed. If so, obtain the pathology report and affix to case report.

- **Cases 55 years of age or older diagnosed with CJD – not deceased**.
  1. Determine if a biopsy or other pathology was performed. If so, obtain the pathology report and affix to case report.
  2. If no laboratory testing has been performed, inform the physician that laboratory services are available for diagnosis from:

National Prion Disease Pathology Surveillance Center
Institute of Pathology, Room 419
Case Western Reserve University
2085 Adelbert Road
Cleveland, Ohio 44106
Phone: 216-368-0587
Web site: **http://www.cjdsurveillance.com** (4/05)

Control Measures

To monitor the prevalence of prion diseases in Missouri and investigate possible cases in which the disease has been acquired from other persons or from animals.

- The Medical Certifier should clearly indicate the diagnosis of CJD on the patient's death certificate when the clinical diagnosis applies because CJD is also monitored from mortality data.
- Performing a brain autopsy in patients with suspected or clinically diagnosed CJD is encouraged to confirm the diagnosis and detect other emerging forms of CJD.
- Free testing is available from the National Prion Disease Pathology Surveillance Center.
- If the NPDPSC arranges the autopsy for you, it will be provided free of charge, including transportation if necessary (Phone: 216-368-0587). The "**Brain Only Autopsy Informed Consent form**" and "**Testing and Reporting Policy form**" are two documents the Center needs families to complete in order to participate in their autopsy program. Also provided is the "**National Prion Disease Pathology Surveillance Center - Autopsy Q & A Sheet**".

For more information on control measures, refer to the following texts:

- Control of Communicable Diseases Manual (CCDM)
- Red Book, Report of the Committee on Infectious Diseases.
- Mandell, Douglas and Bennett's *Principles and Practice of Infectious Diseases*

Laboratory Procedures

For information contact:

National Prion Disease Pathology Surveillance Center
Institute of Pathology, Room 419
Case Western Reserve University
2085 Adelbert Road
Cleveland, Ohio 44106
Phone: 216-368-0587
Web site: **http://www.cjdsurveillance.com** (4/05)

Reporting Requirements

Creutzfeldt-Jakob disease is a Category II disease and shall be reported to the local health authority or to the Missouri Department of Health and Senior Services within three days of first knowledge or suspicion by telephone, facsimile or other rapid communication.

1. For all cases of sporadic CJD, iatrogenic CJD, familial CJD, or variant CJD complete a "Disease Case Report" (CD-1).
2. Contact the Regional Communicable Disease Coordinator immediately for all confirmed, probable, or suspect cases of vCJD.
3. Entry of the complete CD-1 into the MOHSIS database negates the need for the paper CD-1 to be forwarded to the Regional Health Office.
4. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the Regional Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Surveillance Report (CD-51).
5. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the Regional Communicable Disease Coordinator.

References

1. Control of Communicable Diseases Manual. "Creutzfeldt-Jakob Disease." Heymann, David L., ed. 18th ed. Washington, D.C.: American Public Health Association, 2004: 191-194
2. American Academy of Pediatrics. "*Creutzfeldt-Jakob Disease*" In: Pickering, LK, ed. *Red Book: 2003 Report of the Committee on Infectious Diseases.* 26th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2003: 510 - 512.
3. Diagnostic Criteria for Creutzfeldt-Jakob Disease (CJD) Global Surveillance, Diagnosis, and Therapy of Human Transmissible Spongiform Encephalopathies: Report of a WHO Consultation, February 9-11, 1998, Geneva, Switzerland. **http://www.who.int/emc-documents/tse/whoemczdi989c.html** (4/05)
4. National Prion Disease Pathology Surveillance Center, Case Western Reserve University, Cleveland, Ohio, "Glossary." **http://www.cjdsurveillance.com** (4/05)
5. Mandell, Douglas and Bennett's *Principles and Practice of Infectious Diseases*. "Prion Diseases". G. Mandell, J.Bennett, R. Dolin, eds. 6th ed. Vol.2, 2005: 2221-2235

Other Sources of Information

US Food and Drug Administration, Guidance for Industry, "*Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob (CJD) Disease and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products* **http://www.fda.gov/cber/gdlns/cjdvcjdq&a.htm** (4/05; see the Final FDA guidance document.)

The Creutzfeldt-Jakob Disease Foundation, Inc. P.O. Box 5312 Akron, Ohio 44334 (National CJD HelpLine 800-659-1991) **http://www.cjdfoundation.org/** (4/05)

Tyler, Kenneth L., MD., "*Creutzfeldt-Jakob disease*" N Engl J Med. 2003 Feb20;348(8): 681-2

Creutzfeldt-Jakob Disease (CJD)

FACT SHEET

What is Creutzfeldt-Jakob Disease (CJD)?

CJD is a rare, fatal brain disorder that causes a rapid, advancing dementia and associated muscle and nerve disturbances. The disease is often referred to as a subacute spongiform encephalopathy because it usually produces microscopic (sponge-like) holes in the brain.

Who gets CJD?

Anyone can be afflicted with this disease. The disease affects both men and women of various ethnic backgrounds usually between the ages of 50-75 years. Typically, CJD onsets in later life and occurs at approximately 1 case per million annually, worldwide. In the United States there are approximately 250 to 300 new cases per year.

How is CJD transmitted/acquired?

There are three general ways through which CJD can be acquired. First, the disease can occur sporadically (at irregular intervals in persons without known risk factors). **Sporadic CJD** (sCJD) is by far the most common type of CJD and accounts for at least 85% of cases in the United States. Second, the disease can be inherited. About 5-10% of cases in the United States are **inherited CJD** (fCJD). Third, the disease can be acquired through exposure to brain or nervous system tissue/fluids, usually through certain medical procedures. **Iatrogenic CJD** (iCJD - unintended consequence of a medical procedure) has occurred in cases involving corneal transplants, implantation of electrodes in the brain, dura mater grafts, contaminated surgical instruments, and the injection of natural human growth hormone derived from cadaver pituitaries. In other words, one may become infected with CJD from direct contamination with infected neural tissue/fluid.

CJD is not considered contagious in the traditional sense. Spouses and family members who live with CJD patients have not been found to have a greater risk of getting the disease than the general population.

What are the symptoms of CJD?

Initially, persons may have difficulty sleeping, experience depression, problems with muscular coordination, impaired vision, and personality and behavioral changes such as impaired memory, judgment, and thinking. As the disease progresses, mental impairment becomes severe and involuntary muscle jerks (myoclonus) often occur along with blindness. Eventually, the ability to move or speak is lost and the person enters a coma until death occurs.

How soon do symptoms occur?

Generally, onset of symptoms for sporadic and inherited cases occurs about age 60, can be as early as 20 and as late as 90 years. If acquired by surgical procedures such as corneal or dura mater transplants, onset of symptoms can be as short as 16 months or as long as 9 years.

How is CJD diagnosed?

A diagnosis of CJD should be considered when an adult develops rapid dementia with loss of muscle coordination. The only way to confirm a diagnosis of CJD is by brain biopsy or autopsy.

How is CJD treated?

Unfortunately, there is no known effective treatment available to cure or control CJD. Current treatment is aimed at controlling symptoms and making the person as comfortable as possible.

What is variant Creutzfeldt-Jakob disease (vCJD)?

vCJD is a rare and fatal human neuro-degenerative condition. vCJD is thought to be associated with dietary consumption of tissue from cattle infected with bovine spongiform encephalopathy (BSE). Blood transfusion has also been implicated in vCJD transmission in the United Kingdom. vCJD is a new disease, and as of this date only one case has been identified in the United States. vCJD is often confused with classic Creutzfeldt-Jakob (sCJD), but vCJD can be distinguished from sCJD by differences in onset, duration characteristics, and laboratory testing. vCJD cases are generally younger at age of onset, have a longer duration of illness, develop psychiatric signs at presentation, and have distinctive "daisy" plaques. For more information on vCJD, refer to the Variant Creutzfeldt-Jakob Disease (vCJD) Fact Sheet.

Missouri Department of Health and Senior Services
Section for Communicable Disease Prevention
Phone: (866) 628-9891 or (573) 751-6113

Variant Creutzfeldt-Jakob Disease
(vCJD)
FACT SHEET

What is Variant Creutzfeldt-Jakob Disease?
Variant Creutzfeldt-Jakob disease (vCJD) is a rare and fatal human neurodegenerative condition. It is classified as a transmissible spongiform encephalopathy (TSE) because of characteristic spongy degeneration of brain tissue. vCJD is a new disease, and as of this date only one case has been identified in the United States. vCJD is often confused with classic Creutzfeldt-Jakob (sCJD), but vCJD can be distinguished from sCJD by differences in onset, duration characteristics, and laboratory testing. vCJD cases are generally younger at age of onset, have a longer duration of illness, develop psychiatric signs at presentation, and have distinctive “daisy” plaques.

Who gets vCJD?
vCJD affects younger patients (average age 29 years, as opposed to 65 years for sCJD. vCJD has a relatively longer duration of illness with a median of 14 months (as opposed to 4.5 months for sCJD). vCJD is thought to be associated with dietary consumption of tissue from cattle infected with bovine spongiform encephalopathy (BSE). vCJD was first reported in the United Kingdom in 1986.

How is vCJD transmitted/acquired?
The nature of the TSE agent is being investigated and is still a matter of debate. There are several theories under discussion. According to the prion theory, the infective agent is composed largely of a self-replicating protein (prion). Another theory contends that the agent is a "virus-like" agent. The most likely cause of vCJD is exposure to the BSE agent, most plausibly due to dietary contamination by affected bovine central nervous system tissue. Blood transfusions have also been implicated in vCJD transmission in the United Kingdom.

What are the symptoms of vCJD?
Early in the illness, patients usually experience psychiatric symptoms, which most commonly take the form of depression, or a "schizophrenia-like " psychosis. Neurological signs, including unsteadiness, difficulty walking, and involuntary muscle movements develop as the illness progresses. By the time of death, patients become immobile and mute.

How soon do symptoms vCJD occur?
vCJD affects younger patients (average age 29 years) with a relatively long duration of illness (median 14 months).

How is vCJD diagnosed?

Neuropathological diagnosis is mandatory for confirmation of suspected vCJD. Confirmatory examination of the brain should show the following neuropathological features:

- Numerous widespread amyloid plaques surrounded by vacuoles.
- Spongiform change most evident in the basal ganglia and thalamus.
- Prion protein accumulation in high density shown by immunocytochemistry, particularly in the cerebellum.

As with sCJD, the patient is suspect for vCJD when the patient's history reveals a rapid dementia and observed loss of muscle coordination. Confirmation of the disease is done through brain biopsy or autopsy.

How is vCJD treated?

There is no known effective treatment available for vCJD. As with sCJD, treatment is aimed at controlling symptoms and providing comfort measures.

CJD (Sporadic, Inherited, or Iatrongenic)

For more information on CJD, refer to the Creutzfeldt-Jakob Disease Fact Sheet.

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NATIONAL PRION DISEASE PATHOLOGY SURVEILLANCE CENTER

Brain Only Autopsy Informed Consent

I do hereby state that I am the nearest relative or power of attorney for the patient and therefore am legally entitled to and do hereby grant permission for the performance of a brain-only autopsy on this patient as arranged by the National Prion Disease Pathology Surveillance Center (NPDPSC). The samples from this procedure are to be submitted to the NPDPSC for further scientific study and diagnostic purposes.

I further authorize NPDPSC to obtain the patient's medical records from the physicians listed below.

I understand that the results of this research will be released to the physicians noted below, as the NPDPSC is not authorized to release information directly to family members.

SIGNED: _____

PRINTED NAME: _____

TODAY'S DATE: _____

PHONE NUMBER: _____

RELATIONSHIP TO PATIENT: _____

PATIENT NAME: _____

PATIENT DATE OF BIRTH: _____

PHYSICIAN INFORMATION

Physician name	Specialty	Phone number

Patient Information

Race: _____ ❑ Male ❑ Female

City/State of residence: _____

In what month and year did the patient start showing signs of CJD? _____

Is the patient deceased?

- ❒ Yes – If YES, please fill out the information in the box below.
- ❒ No

Date of Death_____ Time of Death _____

City/State of Death _____

Is the patient married?

- ❒ Yes – What is his/her spouse's name? _____
- ❒ No

Where is the patient currently located? _____

What is the phone number? _____

What hospitals was the patient seen at?_____

_____

Does the patient have a known history of foreign travel?

- ❒ Yes: Where? _____
- ❒ No

Does the patient have a known history of hunting or eating wild game?

- ❒ Yes: In what state? _____
- ❒ No

Does the patient have a family history of CJD or early onset dementia?

- ❒ Yes – Please describe: _____
- ❒ No

Contact Information

Who is the primary family contact? _____

What is their relationship to the patient? _____

Main phone: _____ Alternate phone: _____

Has the family selected a funeral home/mortuary/crematory?

- ❒ Yes – If YES, please fill out the information in the box below.
- ❒ No

Name of facility: _____

Contact person: _____

City and state: _____

Phone number: _____

Name of the person who completed this form: _____

Phone number (if not noted above): _____

National Prion Disease Pathology Surveillance Center
Testing and Reporting Policies

As a part of our surveillance efforts for CJD, the National Prion Disease Pathology Surveillance Center (NPDPSC) conducts four different tests on the biopsy and autopsy samples we receive:

- Western blot: This test demonstrates the presence of the abnormal prion protein, which is believed to cause CJD and other prion diseases. If the abnormal protein is present, the case is positive. The Western blot is the most sensitive test for prion disease. This test is performed on frozen tissue.
- Immunohistochemistry (IHC)/Histology: In these tests, the neuropathologist examines slides of specially prepared brain tissue to see where the abnormal prion protein appears in order to help determine the type of prion disease. Different types of CJD have different distribution patterns of the abnormal protein. These tests are performed on fixed tissue.
- Genetic analysis: This test determines if the patient has a genetic mutation, and therefore a familial prion disease. The genetic analysis can only determine if a case is familial (which occurs in about 10% of positive cases); in all other forms of prion disease such as sporadic, iatrogenic, or variant CJD, the genetic analysis may help to identify the specific type. This test is performed on frozen tissue or blood. If we receive sufficient amounts of frozen tissue, blood is not required.

All four of these tests must be performed to provide a full diagnosis. We perform all of them providing that the appropriate samples are available. If one of the samples is not available, we cannot perform all of the tests and cannot provide a full diagnosis.

Although we perform all of the above tests for our important research efforts on prion disease, we realize that some families may not want all of the information we collect. In particular, some families do not want to receive genetic information. Genetic mutations not only affect the patient, but also other blood relatives who could also have the mutation. It is important to discuss the psychological implications, confidentiality and insurance with them to determine if they wish to receive this information.

In order to insure that the family receives only the information they want, we are asking clinicians to consult with families to determine if they would like to receive a full or partial diagnosis. Please indicate their choice on the attached form and fax it to us at **216-368-4090**. The NPDPSC will not release genetic information until this form is returned.

For questions, please contact us at **216-368-0587** or cjdsurv@case.edu.

- ❑ Please send only a partial diagnosis, including the Western blot (if frozen tissue is available) and IHC/Histology (if fixed tissue is available), without the genetic analysis. The partial diagnosis will only tell if the case is positive or negative.
- ❑ Please send the full diagnosis, including the genetic analysis (only available if blood/frozen tissue is submitted). The full diagnosis will tell if the case is positive or negative and provide the type (sporadic and the subtype of sporadic, familial, or variant) of prion disease if the case is positive.

Patient Name: _____

Physician Signature: _____

Date: _____

National Prion Disease Pathology Surveillance Center
Autopsy Q & A

Are we required to have an autopsy conducted in cases of suspected CJD?
Currently, we are not aware of any state that requires autopsy in cases of suspected CJD. However, several states require that the case be reported to the State Department of Health, and they strongly recommend that an autopsy be performed if CJD is suspected by a medical doctor. Your doctor should be able to tell you what is required in your state.

Why should we have an autopsy conducted?

- An autopsy is the only way to confirm the clinical diagnosis of CJD.
- It also is the only way to determine the type of CJD. Most CJD cases are sporadic. Other types of CJD are genetic, iatrogenic, or new variant.
- It helps to further our understanding of CJD. Some day, we hope to be able to successfully treat this disease. In order to reach that goal, we must first understand how the disease works. Tissue acquired at autopsy by the Center is made available to laboratories qualified to do research on prions, helping to reach that goal.

What does the autopsy entail?
We perform brain only autopsies. This means that we will remove the entire brain for analysis. If for some reason you would like to have a full autopsy conducted, please let us know. We will try to make arrangements with the Institution where the autopsy is to be performed.

Will we still be able to have an open casket if we want one?
Only your funeral home can make that decision. However, many of the families who have an autopsy done have been able to have open casket funerals. Our autopsy coordinators are available to address any concerns that your funeral home might have.

How long will it take to have an autopsy performed?
The Center will make every effort to have the procedure completed within a day. However, please note that weekends and holidays can slow the process down. However, the autopsy can be performed with up to a few days delay without jeopardizing the diagnostic examinations.

Can the autopsy be performed locally?
Whenever possible, the Center brings a pathologist to the autopsy location in order to make the process as easy and quick as possible. However, the Center occasionally has to use an out-of-town provider. The Center will make all of the transportation arrangements and cover costs if they are necessary, and works to complete the entire process as soon as possible. The Center will keep you posted if delays are expected so that you can adjust your plans accordingly.

How do we make arrangements for an autopsy if you decide that to have the autopsy done?
Some hospitals will provide autopsy services for their patients. If they do not, the Center will make all of the arrangements. If you would like the Center to make autopsy arrangements for your loved one, call our Autopsy Coordinators at 216-368-0587. All you will need to do is provide some basic information about your loved one and send written consent to perform the autopsy. The Center will take care of everything else.

How much will an autopsy cost?
If the Center arranges the autopsy for you, it will be provided free of charge, including transportation if necessary. Please note that we cannot cover funeral or embalming charges.

Will the Center send us the results?
Our Internal Review Board requires the Center to send the results to a medical doctor only. Often, the Center sends the results to the patient's neurologist or family doctor. You will be asked which doctor you would like to receive the results, and you can change this list at any time. These doctors can discuss the results with you, answer any questions you might have, and consult with you on the next steps. Please note that the Center cannot release the information directly to family members.

How long will it take to get results?
The samples must be treated before they can be safely sent to our facility. On average, most samples arrive to us in about two weeks from the autopsy date. The Center's first test results will be available two weeks from the date of receipt. These preliminary results will tell you if the findings are consistent with prion disease or not, but they will not provide a full or complete diagnosis. The final diagnosis is provided in 1½ to 2 months on average. On rare occasions, the process can take longer, since some cases are challenging. At any time, you can contact the Autopsy Coordinator to learn the status of your case.

What if my loved one turns out not to have CJD?
The Center is willing to send the tissue samples to another facility for analysis or refer you to one of the pathologists at our facility. The Center will do everything possible to support your family in your search for answers. Unfortunately, the family must cover these expenses (if any) for the diagnosis made at other institutions.

What if I have more questions?
If you have any additional questions or would like to discuss your situation with someone at our Center, please call our Autopsy Coordinators at 216-368-0587.